REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
10-08-2011	Final	11/01/2008 to 10/31/2010

4. TITLE AND SUBTITLE
TECHNOLOGY SUPPORT FOR COMBAT CASUALTY RELATED MEDICAL INFRARED IMAGING

5a. CONTRACT NUMBER
FA9550-09-01-0020

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Robert D Pearlstein
Bobby D Guenther

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Duke University,
Research Administration, 2200 W. Main St., Suite 820 Erwin Square Plaza,
Durham, NC 27705;
909-684-5175;

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Air Force Office of Scientific Research
875 North Randolph Street
Suite 325, Rm 3112
Arlington, VA 22203

10. SPONSOR/MONITOR'S ACRONYM(S)
AFOSR

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
AFRL-OSR-VA-TR-2012-0719

12. DISTRIBUTION / AVAILABILITY STATEMENT

Public Release

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Acute Compartment Syndrome (ACS) of the lower extremities is a serious complication that can be limb or even life threatening. The most common causes include fractures and vascular injury, both of which are frequently seen in war wounded soldiers. The present effort was undertaken as part of a collaboration with the Joint Combat Casualty Care Research Team (JC2RT) at Joint Base Balad military hospital to provide training and logistical support for a combat theater study to study the reliability of infrared imaging in identifying wounded US military personnel at risk for developing ACS prior to evacuation to Landstuhl Regional Medicial Center. These efforts were motivated by findings from a study conducted at a US civilian Level I trauma center in which a thermal signature involving the distal lower extremity was shown to reliably identify trauma patients who had or would go on to develop extremity ACS. Patient enrollment in the Balad study has been completed and the JC2RT is currently analyzing the results.

15. SUBJECT TERMS
Acute compartment syndrome; Infrared imaging; telethermography; combat casualty management.

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Robert D Pearlstein
U	U	U	UU	8	19b. TELEPHONE NUMBER *(include area code)* 919-684-6427

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

Final Report: Technology Support for Combat Related Medical Infrared Imaging
Grant/Contract Number: FA9550-09-1-0020
Contract Period: November 1, 2008 – October 31, 2010
PI: Robert D Pearlstein Dept Surgery, Duke University
Co-PI: Bobby D Guenther Dept Physics, Duke University

EXECUTIVE SUMMARY: The present effort was undertaken as part of a collaboration with the Joint Combat Casualty Care Research Team (JC2RT) at Joint Base Balad military hospital to provide training and logistical support for a combat theater study to study the reliability of infrared imaging in identifying wounded US military personnel at risk for developing acute compartment syndrome of the lower extremity (ACSLE) prior to evacuation to Landstuhl Regional Medicial Center. These efforts were motivated by findings from a study conducted at a US civilian Level I trauma center in which a thermal signature involving the distal lower extremity was shown to reliably identify trauma patients who had or would go on to develop extremity ACS. All specific aims of the project were accomplished. Patient enrollment in the Balad study has been completed and the JC2RT is currently analyzing the results. The program is currently being considered for continuation at Kandahar Hospital, Afghanistan.

BACKGROUND: For the last twelve years, we have explored several applications of microbolometer-based (long-wave, 8-14 micron) infrared imaging technology in medicine. Partnering with the U.S. Army Night Vision and Electronics Sensors Directorate at Ft. Belvoir, the Duke University Medical IR group has supported a number of clinical efforts examining the efficacy of IR imagers in diagnosis and/or treatment, particularly in the area of critical care medicine. One of the most successful of these efforts was performed at the University of North Carolina Hospitals, Department of Emergency Medicine, in which a promising new approach was identified for early screening of individuals sustaining lower extremity trauma at risk of developing acute compartment syndrome affecting the lower extremities.

Acute Compartment Syndrome (ACS) of the lower extremities is a serious complication that can be limb or even life threatening. Although ACS can occur within any fascial envelope, the condition most frequently occurs in the muscle compartments of the lower extremity. The most common causes include fractures and vascular injury, both of which are frequently seen in war wounded soldiers.

The underlying issue in all forms of compartment syndrome (CS) involves tissue swelling within a closed space and the resulting compromise of tissue blood flow. When capillary perfusion through the affected compartment is unable to meet the metabolic demands of the tissue due to increasing intracompartmental pressure, irreversible ischemic damage can and will occur if CS is left untreated. Timely diagnosis and treatment of CS can be problematic, especially in patients with multiple trauma or altered mental status. This is true in civilian medical settings, and especially relevant to combat casualty management in which there are additional concerns related to transport of the injured soldiers from the combat theater to Landstuhl Regional Medical Center (LRMC). The precise time interval from the onset of tissue ischemia in compartment syndrome to the development of nerve and muscle necrosis is unknown, but may occur as early as three hours [Vaillancourt, 2004; Whitesides and Heckman, 1996], whereas flight time from medical evacuation facilities in Iraq and Afghanistan to Germany is in the order

of 6-8 hours, with no opportunity for treatment in route. According to statistics we obtained from LRMC, 15 cases of compartment syndrome were diagnosed and treated at LRMC between 1 Jul 07 and 30 Jun 08; likely most of these involved patients transported from combat theater hospitals.

As emphasized in the Joint Theater Trauma System Clinical Practice Guideline for CS in extremity war wounds, there is at present no definitive diagnostic test for CS, and prophylactic intervention (fasciotomy) is now recommended in high risk patients for whom extended monitoring is not possible.[Kragh, 2009] However, there is no clear consensus as to the optimal use of prophylactic intervention given the known risks associated with the surgical treatment. Physical examination continues to be the standard means for establishing the diagnosis of CS, but signs and symptoms may not be present until late in the evolution of the syndrome, when damage is already irreversible. [Matsen, 1980; Mabee and Bostwick, 1993; Tiwari, 2002] Direct measurement of compartment pressures can support the diagnosis, although not all patients with "abnormal" pressure readings go on to develop CS [Janzing and Broos, 2001; Prayson, 2006]. Other instrumental approaches, e.g., near-infrared spectroscopy, Doppler methods, have been proposed, but have yet to be shown superior to direct pressure measurements, nor shown to improve patient outcome.

Based on the findings of a study conducted with the support of the AFOSR at the University of North Carolina Emergency Department [Katz et al 2008, details provided in Preliminary Findings], we have hypothesized that thermal imaging would provide a highly specific and sensitive means for identifying combat casualties who either have developed or who will go on to develop lower extremity CS. With the support of the US Army Night Vision and Electronic Sensor Directorate (Dr. Fenner Milton, NVESD Director) and the AFOSR (Contract FA9550-08-01-0006), we met with AFCENT/SG Staff at Shaw AFB (Col. Bryan Funke) in August of 2008 to discuss our interest in conducting an observational clinical trial at Joint Base Balad Hospital. Maj. Kenneth Egerstrom, who at the time was completing his second year in the USAF RAM program, became interested in this project and agreed to serve as PI for a clinical trial at Balad Hospital. A protocol entitled "Infrared technology as a tool to predict Compartment Syndrome in War Wounded" was submitted to the Joint Base Balad Hospital for review and approval in October 2009.

RATIONALE:

In 2007, we participated in a prospective observational study of medical IR imaging for early detection of acute lower extremity compartment syndrome in trauma patients. The study included a total of 164 patients admitted to the University of North Carolina Emergency Department service [Katz, 2008]. Images were obtained during the patient's initial trauma resuscitation in the ED using a 320x240 long-wave (thermal) IR camera. Subsequently, patients were managed according to standard procedures including as indicated consult with the surgery service for assessment and treatment of compartment syndrome. Four research assistants, blind to the patient's presentation, injury pattern and outcome analyzed the images at a later date. Patients who developed compartment syndrome were identified by review of medical records that reported fasciotomies with an intraoperative diagnosis of CS.

Eleven of the 164 patients in the series were diagnosed with lower extremity compartment syndrome as determined by the attending surgeon according to standard clinical criteria. Four of these patients developed bilateral compartment syndrome. The average time interval between injury and ED admission was 91±67 min (mean +/- SD) for these eleven patients and 93±48 min for the 153 patients who did not develop compartment syndrome. All of the patients diagnosed with compartment syndrome exhibited a distinctive thermal signature involving the dorsal and lateral surfaces of the foot in the affected extremity as shown in the Figure 1 taken at the time of primary resuscitation. The patient in this image was ultimately diagnosed several hours later and treated for bilateral lower extremity compartment syndrome

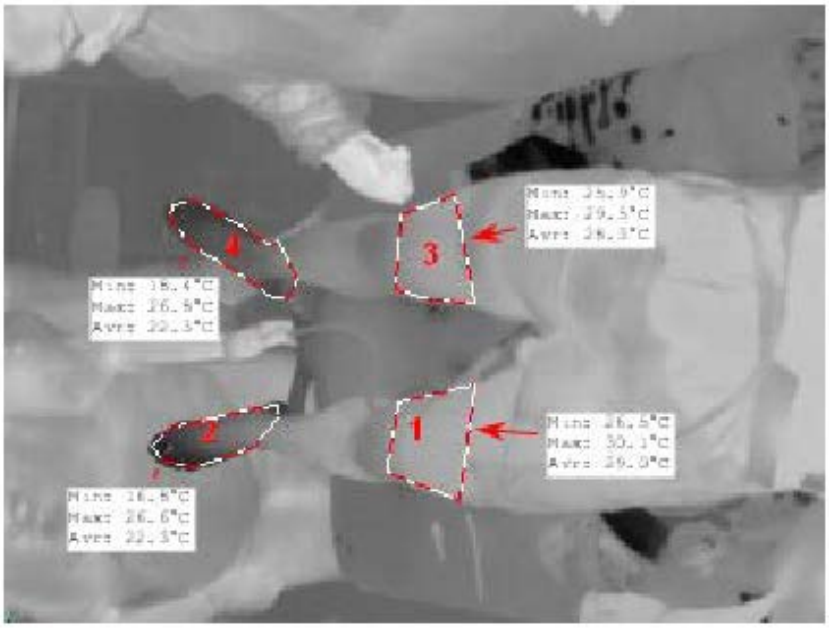

Figure 1: Infrared image of a patient taken during primary resuscitation of a patient admitted to the University of North Carolina Emergency Room in 2007. This patient was later diagnosed with bilateral compartment syndrome. Note the difference in skin surface temperatures of the upper leg and the dorsal surface of the foot and toes. From: Katz, 2008.

From the radiometric images, it was possible to determine the mean temperature of the anterior thigh and foot (regions of interest as shown in Figure 1) for each leg in every patient imaged, as well as a derived index of distal extremity cooling (thigh-foot index, the temperature difference between the measured thigh and foot temperatures in each extremity).

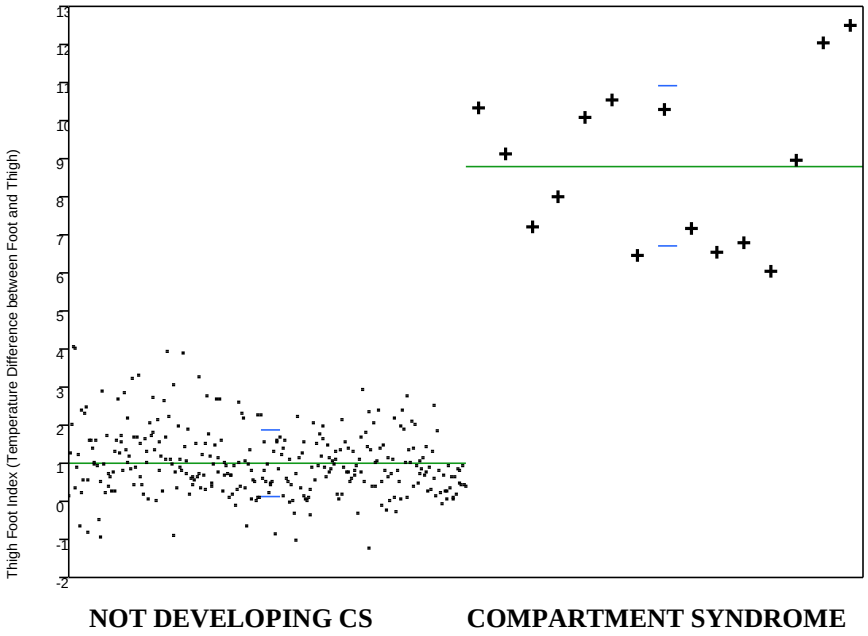

Figure 2. Scatterplot showing individual measurements of the temperature difference between the dorsal surfaces of the thigh and foot separated by clinical outcome from the UNC Study. ΔT for each leg is included as a separate point. From Katz, 2008.

As shown in the scatterplot above (Figure 2), the thigh-foot index (in degrees Centigrade) completely discriminated patients diagnosed with CS from those not developing CS. Bars indicate mean and SD for the respective conditions. Receiver operating characteristic (ROC) curves were assessed as a measure of discrimination efficiency. Thigh-foot index and foot temperature (measured several hours before the clinical diagnosis was made) were both found to have excellent discrimination in identifying patients diagnosed with CS (AUC=1.0 and AUC= 0.98 respectively).

SPECIFIC AIMS

1. To provide technical support for a prospective observational study conducted by the Joint Combat Care Research Team (JC2RT) to evaluate whether IR technology can be used as a non-invasive, predictive tool to discriminate war wounded admitted to the emergency service at Joint Base Balad (JBB, Iraq) Hospital who have or will develop ACS.

2. This support was to include providing infrared technology for deployment to the JC2RT for use in conducting the prospective observational study.

3. This support was to include training members of the JC2RT in the operation of hardware and software in use at JBBH emergency room.

4. This support was to include analyzing images collected at JBBH in accordance with procedures and to measure endpoints used in the UNC Emergency Department study of infrared imaging in trauma patients with acute compartment syndrome.

ACCOMPLISHMENTS:

All specific aims were successfully completed.

A research protocol, "Infrared technology as a tool to predict Compartment Syndrome in War Wounded", was submitted in December 2009 for review by the Brooke Army Medical Center (BAMC) Institutional Review Board. A prospective observational clinical trial was proposed with Maj. Kenneth Egerstrom USAF as overall PI, LtCol. David Trant USAF as On-site PI, and the Duke Medical IR group (Drs. Pearlstein and Guenther) serving as Co-PI's, was approved in January 2009.

As part of an earlier contract with AFOSR (FA9550-08-01-0006), the Duke Medical IR group working in collaboration with the Army Night Vision Laboratories (Ft. Belvoir) and Irvine Sensors Inc (Irvine, CA) assisted with the development of 5 medical infrared imaging systems. Most of the Duke effort involved the development of the software to be used for data collection and encryption. Details of these efforts were supplied in the Final Report FA9550-08-01-006 and available through DTIC.

Figure 3: Infrared imager installation at Joint Base Balad Hospital, CT imaging suite adjoining the emergency room. The uncooled imager and supporting software were developed by Army Night Vision Labs, Irvine Sensors Inc, and the Duke Medical IR group. The customized Irvine Sensors imager is enclosed in an aluminum frame due to HVAC drafts. A sliding aluminum plate is used during external calibration of the imager. The imager is connected to a computer located in the CT control room.

As part of the present effort and based on feedback from the On-Site PI at JBBH, customized mounting hardware was designed and fabricated for installation of two of the medical infrared imaging systems. These systems were placed in the Emergency Department and Radiology CT scanner rooms at Balad hospital (see Figure 3). In addition, a blackbody calibrator, 2 handheld

infrared thermometers, 4 temperature data loggers, and 2 data logging computers (Dell netbooks) were shipped to Balad in February 2009, the latter for use by flight surgeons during the pre-evacuation physicals. Technical support was supplied by phone and email to troubleshoot system malfunctions.

The Duke Medical IR group, coordinating with the U.S. Army Institute of Surgical Research (USAISR), organized bi-annual training sessions on the use of medical IR equipment and details of the approved JBBH Medical IR protocol for the deploying JC2RT (all training sessions have been conducted at the USAISR, San Antonio, Tx). Training sessions also provided an opportunity for members of the JC2RT research teams to use equipment identical to that which was in use at JBBH.

All images collected at JBBH have been sent to Duke, and these images have been analyzed using the same procedures and endpoints established during the UNC study of trauma patients with acute compartment syndrome. Subject enrollment at JBBH has been low due to a shift in combat operations from Iraq to Afghanistan. Ultimately, this led to a relocation of the Balad JC2RT operations to military hospitals in Bagram and Kandahar, and a shift in the governing IRB from BAMC to the Human Research Protections Office of the US Army Medical Research and Materiel Command at Ft. Detrick. Enrollment in the JBBH clinical trial is currently on hold, although the protocol is still active pending completion of data analysis.

Although Duke personnel remain blinded as to the clinical outcomes of the combat wounded who were imaged, the spatial distribution of skin surface temperature observed in the lower extremities of the war wounded soldiers imaged at JBBH were very similar to those observed in the UNC study. Prominent differences in skin temperature between the upper leg and the dorsal surface of the foot and toes were noted in several patients (e.g., Figure 4 left panel), but that was not the case for the majority (e.g., Figure 4 right panel).

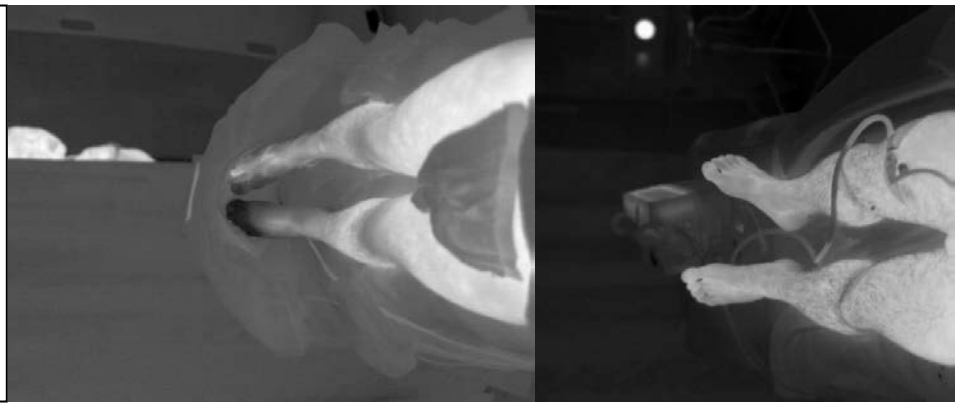

Figure 4. Thermal images of war wounded at Joint Base Balad Hospital. Temperature of the toes and dorsum of the foot were clearly cooler than that of the dorsal thigh in some (right panel, left leg) but not all of the patients examined (e.g. right panel).

In the UNC study, the mean difference in skin temperature measured at the thigh and foot (thigh-foot index, TFI) was found to provide a sensitive and reliable indicator of emergent acute compartment syndrome. The average TFI for the affected leg in the eleven patients in the UNC study who were confirmed to have developed one or more of the physical signs and symptoms (the 6 P's of ACS: pain, paresthesia, pallor, pressure, paralysis, loss of pulse) and ultimately

treated for acute compartment syndrome was 8.8±2.1ºC. Nearly a quarter of the combat casualties imaged at JBB were observed to have a TFI > 8.8 ºC in at least one lower extremity.

CONCLUSIONS: The results of the JBBH infrared imaging study are still being analyzed. The study was designed for a total enrollment of approximately 850 subjects in order to obtain a statistical measure of the efficacy of infrared imaging in predicting acute compartment syndrome. Additional subject enrollment is anticipated once a protocol is approved for transfer to Afghanistan. We are currently assisting with the preparation of the clinical protocol for Kandahar Hospital and anticipate that the clinical study will be completed as originally undertaken. Compartment syndrome remains a serious complication that is common after the types of injuries seen in combat wounded. The ultimate goal of the ongoing research effort will be a prospective, randomized clinical trial to determine if early intervention based on thermographic imaging findings leads to improved patient outcome.

COLLABORATORS: LtCol. Kenneth Egerstrom, USAF; LtCol. David Trant, USAF; Dr. Larry Katz, Department of Emergency Medicine, University of North Carolina Hospitals; Col. Byron Funke, USAF; Dr. David Randall, USArmy Night Vision Laboratories (Ft. Belvoir); Mr. Wayne Antesberger, USArmy Night Vision Laboratories (Ft. Belvoir); Mr. Dean Kissinger, USArmy Night Vision Laboratories (Ft. Belvoir); Mr. Alexander Finch, Department of Surgery, Duke University School of Medicine.

PUBLICATIONS: None

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